

## Melanotan Tanning Injection: A Rare Cause of Priapism



Chase W. Mallory, BHS,<sup>1</sup> Diana M. Lopategui, MD,<sup>2</sup> and Billy H. Cordon, MD<sup>2</sup>

### ABSTRACT

Melanotan II, an injectable melanocortin analog, is illicitly available on the internet to generate a sunless tan through melanocyte induction. It is also used as a sexual stimulant in unlicensed performance enhancement clinics, and has been investigated as a possible treatment agent in erectile dysfunction. We describe in this case report a patient presenting with acute ischemic priapism after subcutaneous injection of melanotan II. The patient was initially managed with cavernosal aspiration and irrigation, and intracavernous injection of phenylephrine without achieving detumescence. After failing initial management, the patient underwent operative management with penoscrotal decompression, a promising alternative technique for the management of refractory ischemic priapism. Priapism after melanotan II injection has only been reported in the literature twice before. This case report highlights a rare presentation of acute ischemic priapism after melanotan II use, managed with surgical decompression. Future therapeutic applications of these agents and updated management guidelines should consider priapism as a possible side effect. **CW. Mallory, DM Lopategui, BH. Cordon. Melanotan Tanning Injection: A Rare Cause of Priapism. Sex Med 2021;9:100298.**

Copyright © 2020, The Authors. Published by Elsevier Inc. on behalf of the International Society for Sexual Medicine. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

**Key Words:** Melanotan; Melanocortin; Priapism; Penoscrotal Decompression; Erectile Dysfunction

### INTRODUCTION

Melanotan products can be purchased over the internet illegally to induce melanocyte production and create sunless tanning. Melanocortin products act on melanocortin (MC) receptors in the skin to stimulate eumelanin and hyperpigmentation (MC-1) as well as in the central nervous system, causing sexual arousal and spontaneous erection (MC-3 and MC-4)<sup>1</sup>. Certain formulations of melanotan have been studied as potential modulators of sexual function in men and have been noted as a treatment of erectile dysfunction at certain doses.<sup>2</sup> Only 2 case reports have documented melanotan-induced priapism.<sup>1,3</sup>

Priapism is defined as an erection lasting longer than 4 hours, unrelated to sexual stimulation.<sup>4</sup> Ischemic priapism, also known as vaso-occlusive or slow flow priapism, is a relatively uncommon medical emergency which can progress to fibrosis of cavernosal tissue and erectile dysfunction.<sup>4</sup> The literature related to management of priapism is not extensive, mostly consisting of case

reports and small case series rather than prospective studies. Likewise, the American Urology Association Guidelines for priapism have not been updated in over a decade,<sup>4</sup> reflecting the paucity of research and innovation in its management. Traditionally, various shunt procedures as well as immediate penile prosthesis placement have been used for surgical management of ischemic priapism. Recent data on penoscrotal decompression (PSD) has shown promising outcomes as a viable salvage or alternative strategy for management of refractory ischemic priapism and has become our preferred technique.<sup>5</sup>

We report a priapism case presenting with a unique etiology, with an unelucidated mechanism of action. Our aim is to promote education to both patients and clinicians regarding this rare side effect of melanotan II (MT II), as well as integrate MC analogs into the risk assessment of use of drugs that may precipitate priapism.

### CASE PRESENTATION

A 55-year-old Caucasian man presented to our institution's emergency department with a chief complaint of painful, sustained penile erection of 30 hours of duration on arrival. The onset of priapism was after self-administration of a subcutaneous injection of 2 mg of MT II (MC) to the abdomen. There was no preceding trauma, sexual stimulation or concomitant other drug use. The patient had used MC before for over 6 years, in an effort to darken his skin each year before summer. He reports it typically caused him an erection lasting a few minutes after

Received October 19, 2020. Accepted December 1, 2020.

<sup>1</sup>Herbert Wertheim College of Medicine, Florida International University, Miami, FL, USA;

<sup>2</sup>Division of Urology, Mount Sinai Medical Center, Miami, FL, USA

Copyright © 2020, The Authors. Published by Elsevier Inc. on behalf of the International Society for Sexual Medicine. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

<https://doi.org/10.1016/j.esxm.2020.100298>

injection, which detumesced spontaneously in prior uses of the drug. He also reported severe nausea with its use, and so each year he injected once before bedtime. He reports no prior history of priapism or erectile dysfunction.

On examination, the patient had a rigid, very tender penis. He was initially managed at bedside with intracavernosal injection of phenylephrine in sequential increments of 500mcgs, up to a total of 4,500mcgs. Phenylephrine injections were alternated with intracavernosal irrigation of saline, with removal of about 150 cc of very dark blood. Patient tolerated the procedure well with blood pressure below 150/90 mmHg at all times. On multiple occasions the patient's erection visibly decreased but retumesced within a couple minutes. Given the prolonged time of ongoing priapism, in addition to the persistence of a 10/10 rigid erection despite pharmacological and bedside irrigation management, decision was made to proceed with surgical management with PSD.

The patient was brought to the operating room and general anesthesia was induced. After shaving, prepping and draping of the penoscrotal area in the usual sterile fashion, a Foley catheter was placed. A midline penoscrotal incision was made and brought down to the tunica albuginea. After placement of stay sutures on bilateral corpora, corporotomies were made with immediate corporal bleeding. A pediatric Yankauer was introduced into the corporal bodies and driven both proximally and distally. The corpora were then irrigated copiously with saline. Complete resolution of the erection was noted and bright red blood was seen. Running 2-0 absorbable suture was used to close the corporotomies and the incision was closed in layers. On postoperative day 1 he had retumesced slightly more than what we normally expect after PSD, so he was observed one additional day and discharged on postoperative day 2 with pain control.

At 15 week follow-up, he reported a degree of new onset erectile dysfunction, with rigidity 4/10 and corpora fibrosis on examination, with no penile curvature. He has attempted PDE5 inhibitors with no response, and is pending penile Doppler ultrasound for evaluation before further treatment.

## DISCUSSION

An otherwise healthy 55-year-old man with no prior history of priapism or sexual dysfunction presented with a painful sustained erection after subcutaneous injection of MT II to the abdomen. After failing non-operative management he was taken to the operating room for PSD. On follow-up, his erectile function was poorer than our previously performed PSDs for more common etiologies of priapism. Although his PSD resulted in complete resolution of the erection initially, he was observed for an additional day given he had retumesced slightly more than what we normally expect after a PSD. Given his pain was controlled, he was discharged and no further interventions were performed. However we suspect the half-life

of MT II is long and possibly led to some ongoing ischemia resulting ultimately in worsened erectile function, particularly when comparing it with other patients who have undergone a PSD.

There are only 2 previous case reports on MC-induced priapism in the literature.<sup>1,3</sup> Nelson et al<sup>3</sup> described a case in which 6 mg of MT II was injected subcutaneously concomitantly with an unspecified "pain pill", resulting in systemic toxicity with sympathomimetic excess, renal dysfunction, and rhabdomyolysis. The patient was managed in the ICU for 3 days receiving lorazepam, IVF, and sodium bicarbonate. In addition, Dreyer et al presented a case of melanotan-induced ischemic priapism after subcutaneous abdominal injection of one "phial" (unknown dose) as recommended per the seller.<sup>1</sup> Detumescence was achieved after surgical intervention with a Winter's shunt after failing phenylephrine intracavernosal injection of 1,000 mcg. Our case presentation is unique in that a relatively small (2 mg) subcutaneous injection of MT II resulted in priapism that required more aggressive treatment with a PSD, after failing to achieve detumescence with maximum intracavernosal phenylephrine and bedside irrigation. This decision was made following our institution's evolved algorithm for management of priapism with PSD. We favor PSD over distal shunts based on our experience and early multi-institutional data showing its safety, efficacy, and promising outcomes.<sup>5</sup> Interestingly, the patient had tolerated the same dose for 6 years in a row without experiencing priapism or any other adverse effect.

Melanotan products (promoted as a Barbie Doll drug) have been implicated in sunless tanning, sexual stimulation and weight loss.<sup>3</sup> However, they have been associated with unwanted side effects including nausea, fatigue, flushing, dizziness, and sympathetic stimulation. These products are synthetic analogs of  $\alpha$ -melanocyte stimulating hormone, which bind to G-protein coupled melanocortin-1 (MC-1) which activates tyrosinase and melanogenic enzymes, thus increasing skin pigmentation.<sup>3</sup> Melanotan is most popularly injected subcutaneously for maximum skin darkening effects, although it may be administered intravenously as well.<sup>3</sup>

The three melanotan products currently available include MT I, MT II, and bremelanotide. Clinical trials of MT I show an increase in skin pigmentation, with UVB radiation and sunlight having a synergistic effect.<sup>3</sup> MT I is labeled as having a relatively benign safety profile, with a similar side-effect profile noted above including potential changes to pre-existing melanocytic nevi, with no known progression to melanoma documented in the literature.<sup>3</sup> MT II has been shown to be just as effective as MT I in terms of tanning, with broader ranging effects through the stimulation of MC-3, MC-4, and MC-5 receptors.<sup>3</sup> In addition to its melanogenic effects, MT II has the ability to induce erections, and to act as a sexual stimulant in both men and women through its action on MC-3 and MC-4 receptors.<sup>3</sup> For this reason, an MT II metabolite known as bremelanotide has been developed for use as sexual stimulant without the

associated tanning effects.<sup>3</sup> Clinical trials of bremelanotide were halted because of concerns of increased blood pressure in patients.<sup>3</sup> Other side effects of MT II and its derivatives include nausea, fatigue, yawning and lipolysis.<sup>3</sup> Clinical trials are also investigating the role of the MC-4 receptor in monogenic obesity.<sup>6</sup> The efficacy and safety of MC-4 agonist, setmelanotide, is being explored in the treatment of obesity and hyperphagia.<sup>7</sup>

Currently melanotan products are under clinical investigation and are not licensed for use on the general public. The Food and Drug Administration and multiple European governing authorities have warned against the use and sale of melanotan.<sup>3</sup> In the United States, purchasing melanotan products is easily accessible, unregulated, and potentially dangerous. The purity and dosing of the drugs is unknown, and there is little data to support the doses recommended by the websites selling the product.<sup>3,7</sup> The side-effect profile and duration of MC analogs are highly variable and unknown. Some case reports with severe side effects such as sympathomimetic overdrive and, in this case, acute ischemic priapism, raise concern for their use without proper physician monitoring.

## CONCLUSION

Melanotan, an injectable MC analog, is illicitly available on the internet to supplement sunless tan, sexual arousal, and weight loss. We report a rare case of a patient presenting with priapism after subcutaneous injection of melanotan. The association with MC analogs and painful erection encourage its role as a screening tool in the history of individuals presenting with priapism. Although the prevalence of melanotan use is currently unknown, further research is necessary to quantify use of MC-induced priapism in higher-risk populations seeking its utility as a sunless tanning agent.

**Corresponding Author:** Chase Mallory, BHS, Department of Translational Medicine, Herbert Wertheim College of Medicine, Florida International University, 2272 SW 19th Street, Miami, FL, 33145, USA. Tel: 7274092747; Fax: 305-348-0650; E-mail: [Cmall024@fiu.edu](mailto:Cmall024@fiu.edu)

*Conflicts of interest:* The authors have no conflicts of interest to disclose.

*Funding:* None.

## STATEMENT OF AUTHORSHIP

Chase W. Mallory: Writing - Original Draft, Formal Analysis, Project Administration, Conceptualization, Resources, Writing - Review & Editing. Diana M. Lopategui: Conceptualization, Methodology, Investigation, Resources, Writing - Review & Editing, Funding Acquisition, Writing - Original Draft, Formal Analysis, Project Administration. Billy H. Cordon: Conceptualization, Methodology, Investigation, Resources, Writing - Review & Editing, Funding Acquisition, Writing - Original Draft, Formal Analysis, Project Administration.

## REFERENCES

1. Dreyer BA, Amer T, Fraser M. Melanotan-induced priapism: a Hard-Earned tan. *BMJ Case Rep* 2019;12:e227644.
2. Hadley ME. Discovery that a melanocortin Regulates sexual functions in male and female Humans. *Peptides* 2005; 26:1687-1689.
3. Nelson ME, Bryant SM, Aks SE. Melanotan II injection resulting in systemic toxicity and Rhabdomyolysis 2012. *Clin Toxicol* 2012;50:1169-1173.
4. Monague DK, Jarrow J, Broderick GA, et al. Guideline on the management of priapism. *J Urol* 2003;170 (4 Pt 1):1318-1324.
5. Baumgarten AS, VanDyke ME, Yi YA, et al. Favorable multi-institutional experience with penoscrotal decompression for prolonged ischemic priapism. *BJU Int* 2020;126:441-446.
6. U.S. National Library of Medicine. Role of the melanocortin-4 receptor in Hypoactive sexual Desire Disorder. <https://clinicaltrials.gov/ct2/show/NCT04179734>. Accessed July 1, 2020.
7. U.S. National Library of Medicine. Setmelanotide (RM-493), melanocortin-4 receptor (MCR4) agonist, in Bardet-biedl Syndrome (BBS) and Alstrom Syndrome (AS) patients with Moderate to severe obesity. <https://clinicaltrials.gov/ct2/show/NCT03746522>. Accessed July 1, 2020.